Hepatitis C Virus (HCV) Epidemiology in the United States: Emerging Trends

Scott Holmberg, MD, MPH
Chief, Epidemiology and Surveillance Branch, DVH, CDC

sdh1@cdc.gov
Presenter Disclosures

Scott Holmberg, MD, MPH

(1) The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose
A Tale of Two Epidemics

• **Chronic HCV**: Rapidly increasing mortality and morbidity

• **Acute HCV**: The “emerging” epidemic of new HCV infections in young persons who inject drugs (PWIDs)
Somewhat declining prevalence, but still 3.2m HCV-infected US residents, 75% born between 1945-1965 ('Baby Boomers’)

From: MM Denniston et al *Ann Intern Med* 2014; 160:293-300
Annual age-adjusted mortality rates from hepatitis B and hepatitis C virus and HIV infections listed as causes of death in the United States between 2000-2013

And this continues to increase “under the radar”

**Figure.** Annual number of deaths from hepatitis C virus and all other 60 nationally notifiable infectious conditions* listed as multiple causes of death in the United States between 2003 and 2013.

* 61 infectious conditions, as reported to CDC
Hidden Mortality From HCV is Increasing: Data from the Chronic Hepatitis Cohort Study (CHeCS)*

- 1600 deaths in well-characterized HCV patients, 2006-2010
- Mean age at death – 59 years
- Under counted by vital records: Only 19% of HCV patients who died had HCV noted anywhere on their death certificates….and this was despite that >75% had pre-mortem evidence of liver disease
- Implies >100 000 deaths/yr--- >75 000 attributable to HCV—in HCV-infected persons in US

The new all-oral medicines for HCV

• One pill/day for 12 weeks cures >95% people
• However, a pill originally cost $1,000 each, thus over $84,000 for a complete course
• While total treatment costs have now been negotiated by most insurers < $50,000 for a complete course—which, incidentally, is what previous less effective therapies cost-- this still is a staggering cost burden given the many HCV patients
“Highest Priority” for Treatment (High risk for mortality/morbidity)

- Advanced fibrosis (Metavir F3) or compensated cirrhosis (F4)
- Organ transplant
- Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis)
- Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

“High Priority” for Treatment (High Risk for Complications)

- Fibrosis (Metavir F2)
- HIV-1 coinfection
- Hepatitis B virus (HBV) coinfection
- Other coexistent liver disease (eg, [NASH])
- Debilitating fatigue
- Type 2 Diabetes mellitus (insulin resistant)
- Porphyria cutanea tarda
So, in 2015, we are kind of “stuck”

• **One side**: treatment even at $ 84k per patient is cost-effective

• **Other side**: we do not have funds to treat 3.2 million at this drug cost

• However:
  – We all agree to treat sickest first
  – Drug prices have come down
  – Cost-effectiveness analysis indicates if we can get prices below $30,000 it would make sense to treat everyone
**Calculating Numbers at “Highest” and “High” Priority for Treatment**

**U.S. household population with chronic HCV infection**

2.7 million*

HCV diagnosed (50%)

1.35 million**

Staged by biopsy or laboratory data available to calculate a FIB-4 score (94%)

1.27 million

- Biopsy (22%): 297,000
- FIB-4 score*** only (72%): 972,000

Meet AASLD/IDSA/IAS-US “highest priority” or “high priority” treatment criteria (64%)

813,000

- Highest priority
  - Metavir F3 or higher (33%): 419,000
  - Lower than F3 with kidney disease (3%): 38,000
- High priority
  - Metavir F2 (22%): 280,000
  - Less than F2 with chronic condition (6%): 76,000


FIB-4 score = [age x AST (IU L⁻¹)]/[platelet (10³ µL⁻¹) x ALT½ (IU L⁻¹)]; FIB-4 score ≥ 2.5 is predictive of advanced fibrosis Metavir F3 or higher, while a FIB-4 score ≥ 1.6 but less than 2.5 is predictive of advanced fibrosis Metavir F2.

Frequent barriers to treatment: No alcohol or drugs in previous 6 months. Some states require biopsies for fibrosis scoring or finding a ‘Fibroscan’ machine to document liver fibrosis/cirrhosis: this is often a barrier. For those in more rural areas, finding a specialist, as required by many state Medicaid offices, can be very difficult.
Improving the HCV Test and Cure Continuum: current efforts to intervene at each of these steps

From: SD Holmberg et al, *NEJM* 2013; 368:1859-62, based on data from CHeCS and NHANES
The Second “Emerging” Epidemic….

- Increasing HCV in young persons…in places we didn’t expect…
Figure 4.1. Reported number of acute hepatitis C cases — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)
Figure 4.2. Incidence of acute hepatitis C, by age group — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)
Figure 4.3. Incidence of acute hepatitis C, by sex — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)
Figure 4.4. Incidence of acute hepatitis C, by race/ethnicity — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)
Of the 34 states that reported to CDC in both 2006 and 2012:

- 30 states reported increases
- 15 states reported >200% increase
- 50% of cases were younger than 30 years

Greatest HCV increase seen in non-urban—especially, rural and Appalachian counties-- east of the Mississippi

From: Suryaprasad et al, *Clin Infect Dis* 2014; 59:1411-9
Trends observed in Massachusetts, Wisconsin, Michigan, and Ohio (‘ELC Studies’)

- These PWIDs were mainly:
  - young (aged 20-29 yrs);
  - white; roughly equal gender distribution
  - non-urban (suburban, rural); and
  - previous oral prescription opioid users (‘Oxycontin’/ oxycodone) users, who transitioned to injecting heroin
<table>
<thead>
<tr>
<th>Drug</th>
<th>N</th>
<th>%</th>
<th>Mean age started</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>413</td>
<td>91%</td>
<td>14.1 years old</td>
</tr>
<tr>
<td>Alcohol</td>
<td>379</td>
<td>83%</td>
<td>15.2 years old</td>
</tr>
<tr>
<td>Powder Cocaine</td>
<td>324</td>
<td>71%</td>
<td>17.4 years old</td>
</tr>
<tr>
<td>Any prescription opioid drugs</td>
<td>345</td>
<td>76%</td>
<td>17.7 years old</td>
</tr>
<tr>
<td>‘Oxycontin’ or oxycodone</td>
<td>337</td>
<td>74%</td>
<td>17.9 years old</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>134</td>
<td>29%</td>
<td>18.7 years old</td>
</tr>
<tr>
<td>Crack cocaine</td>
<td>245</td>
<td>54%</td>
<td>18.8 years old</td>
</tr>
<tr>
<td>Methadone</td>
<td>161</td>
<td>35%</td>
<td>19.3 years old</td>
</tr>
<tr>
<td>Heroin</td>
<td>280</td>
<td>61%</td>
<td>19.7 years old</td>
</tr>
</tbody>
</table>

These cases reported to CDC represent the “tip of the iceberg”

- Our recent best calculation is that each acute HCV case reported to CDC represents at least 13.2 actual cases*

- Thus, we estimate about 30,000 new HCV infections each year currently (mostly in those < 30 yo)

Trends in incidence of acute hepatitis C among young persons reported to CDC, by urbanicity, 2006–2012.

The Non-urban Outbreak is Occurring in Tandem with Ongoing Urban Outbreaks

Acute HCV Cases Reported to CDC in 2013*

<table>
<thead>
<tr>
<th>State</th>
<th>No. Cases</th>
<th>(rate†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kentucky</td>
<td>226</td>
<td>(5.1)</td>
</tr>
<tr>
<td>Indiana</td>
<td>175</td>
<td>(2.7)</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>174</td>
<td>(0.9)</td>
</tr>
<tr>
<td>Florida</td>
<td>134</td>
<td>(0.7)</td>
</tr>
<tr>
<td>New York</td>
<td>131</td>
<td>(0.7)</td>
</tr>
<tr>
<td>Ohio</td>
<td>116</td>
<td>(1.0)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>106</td>
<td>(1.2)</td>
</tr>
<tr>
<td>Tennessee</td>
<td>98</td>
<td>(1.5)</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>81</td>
<td>(0.6)</td>
</tr>
<tr>
<td>North Carolina</td>
<td>79</td>
<td>(0.8)</td>
</tr>
<tr>
<td>Michigan</td>
<td>74</td>
<td>(0.7)</td>
</tr>
</tbody>
</table>

* From: DVH Surveillance Summary 2013
† per 100,000 population
The Epidemiologic “W’s” as we understand them:

- **Who**: young, usually under 30 yo, often under 24 yo; mainly white, non-minority, roughly equal gender distribution
- **What**: Injection of heroin or dissolved oral prescription opioids
- **Where**: Biggest increase in rural and suburban areas, esp east of the Mississippi. However, also some increase seen in urban areas
Next “W”: What’s next?

Future work needs to move forward with focus on how to:

- Get all identified PWIDs to opioid substitution treatment (OST) centers or to needle/syringe exchange programs (NSEPs);
- Get all HCV-infected PWIDs linked to care for their HCV and other infections
There are many barriers to addressing the largest infectious disease epidemic in the United States

- **Clinician attitudes**: this is a ‘benign’ chronic condition

- **Patient issues**: many barriers, including personal

- **Public attitudes**: “AIDS Fatigue” (*add*: Ebola, SARS, pandemic flu, etc). Also, reluctance to help injection drug users

- **Political attitudes**: No strong advocacy: most HCV patients are PWIDs formerly
Summary

• Hepatitis C is the largest, if unappreciated, infectious disease epidemic in the United States

• Deaths in chronic HCV-infected persons far outstrip deaths from HIV and 60 other infectious conditions reportable to CDC

• We are in the midst of an “emerging” epidemic of acute HCV in young non-urban persons who transition from prescription oral opioids to injectable heroin, often in their teens

• Control of the ‘chronic’ and the ‘acute’ outbreaks will require a multipronged approach along a testing-to-cure continuum of care
Thank you

- Epidemiology and Surveillance Branch, Division of Viral Hepatitis, CDC:
  - Scott Holmberg, MD, Chief: sdh1@cdc.gov
  - Fujie Xu, MD, Epidemiology Team Lead: fax1@cdc.gov
  - Ruth Jiles, PhD, Surveillance Team Lead: rxg0@cdc.gov